CLAIMS

WHAT IS CLAIMED IS:

1. An isolated monoclonal antibody comprising a heavy chain variable region comprising FRI, CDRI, FR2, CDR2, FR3, CDR3 and FR4 sequences and a light chain variable region comprising FRI, CDRI, FR2, CDR2, FR3, CDR3 and FR4 sequences, wherein: (a) the heavy chain variable region CDR3 sequence is selected from SEQ ID NO: 3, and conservative modifications thereof; (b) the light chain variable region CDR3 sequence is selected from SEQ ID NO: 6, and conservative modifications thereof.

2. The isolated antibody of claim 1, wherein the heavy chain variable region CDR2 sequence is selected from SEQ ID NO: 2, and conservative modifications thereof, and the light chain variable region CDR2 sequence is selected from SEQ ID NO: 5 and conservative modifications thereof.

3. The isolated antibody of claim 1 or 2, wherein the heavy chain variable region CDRl sequence is selected from SEQ ID NO: 1, and conservative modifications thereof, and the light chain variable region CDR1 sequence is selected from SEQ ID NO: 4 and conservative modifications thereof.

4. The isolated antibody of any one of claims 1-3, which binds to human alpha V integrin subunit with a KD of 10^{-8} M or less.

5. The isolated antibody of any one of claims 1-4, wherein the heavy chain variable region FRI, FR2, FR3 and FR4 sequences are derived from the heavy chain CNTO 95 germline sequence.

6. The isolated antibody of any one of claims 1-5, wherein the light chain variable region FRI, FR2, FR3 and FR4 sequences are derived from the light chain CNTO 95 germline sequence.

7. An isolated monoclonal antibody comprising a heavy chain variable region and a light chain variable region, wherein: (a) the heavy chain variable region comprises an amino acid sequence consisting of SEQ ID NO: 7, and sequences that are at least 80% homologous to SEQ ID NO: 7; (b) the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 8, and sequences that are at least 80% homologous to

SEQ ID NOs: 8 and; (c) the antibody binds to human alpha v integrin subunit with a K_D of 10^{-8} M or less.

8. The isolated antibody of claim 7, wherein the antibody binds to human alpha V integrin subunit with a K_D Of 10^{-9} M or less.

9. An isolated monoclonal antibody comprising a heavy chain variable region derived from the heavy chain CNTO 95 germline sequence (SEQ ID NO:7) and a light chain variable region derived from the light chain CNTO 95 (SEQ ID NO:8) germline sequence, wherein: (a) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 7 or a sequence that is at least 80% homologous to SEQ ID NO: 7; (b) the light chain variable region comprises the amino acid sequence of SEQ ID NO: 8 or a sequences that is at least 80% homologous to SEQ ID NO: 8; (c) the antibody binds to human alpha V integrin subunit with a KD of 10^{-8} M or less.

10. An isolated anti-alpha-V subunit monoclonal antibody, comprising at least one variable region comprising SEQ ID NO:7 or 8.

11. An isolated human monoclonal antibody comprising human heavy chain and human light chain variable regions comprising the amino acid sequences shown in SEQ ID NO: 7 and SEQ ID NO: 8, respectively.

12. An isolated monoclonal antibody that competes for binding to human alpha V integrin subunit with the monoclonal antibody of any one of the preceding claims.

13. An isolated human antibody of any one of the preceding claims produced by a hybridoma, wherein the hybridoma is prepared from a B cell obtained from a transgenic non-human animal having a genome comprising a human heavy chain transgene or transchromosorne and a human light chain transgene or transchromosome, fused to an immortalized cell.

14. An alpha-V subunit antibody according to any one of the preceding claims, wherein said antibody substantially neutralizes at least one activity of at least one alpha-V subunit protein.

15. The antibody of any one of the preceding claims which completely inhibits M21 cell adhesion to vitronectin.

16. The antibody of any one of the preceding claims, comprising a human IgG heavy chain and a human kappa light chain.

17. The antibody of any one of the preceding claims, comprising an IgGl or IgG3 heavy chain.

18. The antibody of any one of the preceding claims, which is a human antibody.

19. A pharmaceutical composition comprising the antibody of any one of the preceding claims and a pharmaceutically acceptable carrier.

20. A composition comprising at least one isolated mammalian anti-alpha-V subunit antibody having at least one variable region comprising SEQ ID NO:7 or 8, and at least one pharmaceutically acceptable carrier or diluent.

21. A composition according to claim 19 or 20, further comprising at least one composition comprising an effective amount of at least one compound or protein selected from at least one of a detectable label or reporter, an anti-neoplastic agent, a TNF antagonist, an antirheumatic, a muscle relaxant, a narcotic, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anethetic, a neuromuscular blocker, an antimicrobial, an antipsoriatic, a corticosteriod, an anabolic steroid, an erythropoietin, an immunization, an immunoglobulin, an immunosuppressive, a growth hormone, a hormone antagonist, a reproductive hormone antagonist, a hormone release modulator, a hormone replacement drug, , an antidepressant, an antipsychotic, a stimulant, an asthma medication, a beta agonist, an inhaled steroid, an epinephrine or analog, a cytokine, or a cytokine antagonist.

22. A composition according to claim 19 wherein the antibody is combined with an anti-neoplastic agent selected from a radiopharmaceutical, an estrogen receptor modulator, a retinoid, a topoisomererase inhibitor, a cytotoxin, an alkylating agent, a nitrogen mustard, a nitrosourea , an antimetabolite, a mitotic inhibitor, and a radiosensitizer.

23. A composition according to claim 22 wherein the anti-neoplastic agent is dacarbazine.

24. An immunoconjugate comprising the antibody according to any one of the preceding claims linked to a therapeutic agent.

25. The immunoconjugate of claim 24 wherein the therapeutic agent is a cytotoxin.

26. The immunoconjugate of claim 25 wherein the therapeutic agent is a radioisotope.

27. A pharmaceutical composition comprising the immunoconjugate of any one of claims 24-26 and a pharmaceutically acceptable carrier.

28. An isolated nucleic acid molecule encoding the antibody of any one of the preceding claims.

29. The isolated nucleic acid molecule of claim 28 wherein the nucleic acid molecule is incorporated into an expression vector.

30. An isolated nucleic acid encoding at least one isolated anti-alpha-V subunit antibody having at least one variable region comprising SEQ ID NO:7 or 8.

31. An isolated nucleic acid vector comprising an isolated nucleic acid according to claim 28.

32. A transfectoma comprising the isolated nucleic acid of claim 28 or 30.

33. A prokaryotic or eukaryotic host cell comprising an isolated nucleic acid according to claims 28, 29, 30 or 31.

34 A host cell according to claim 33, wherein said host cell is at least one selected from COS-1, COS-7, HEK293, BHK21, CHO, BSC-1, Hep G2, 653, SP2/0, 293, HeLa, myeloma, lymphoma cells, Perc.6, or any derivative, immortalized or transformed cell thereof.

35. A method for producing at least one anti-alpha-V subunit antibody according to any of claims 1-18, comprising translating a nucleic acid according to claims 28, 29, 30 or 31 under conditions in vitro, in vivo or in situ, such that the alpha-V subunit antibody is expressed in detectable or recoverable amounts.

36. A transgenic nonhuman animal which expresses a human antibody of any one of the preceding claims, wherein the transgenic non-human animal has a genome comprising a human heavy chain transgene or transchromosome and a human light chain transgene or transchromosome.

37. A method of inhibiting growth of a cell expressing alpha v integrin subunit, comprising contacting the cell with an effective amount of an antibody according to any one of the preceding claims such that the growth of the cell is inhibited.

38. A method according to claim 37, wherein said effective amount is 0.001-50 mg/kilogram of said cells.

39. A method of treating or preventing a disease characterized by growth or metastasis of tumor cells, in a subject comprising administering to a subject the antibody of any one of the preceding claims in an amount effective to treat or prevent the disease.

40. The method of claim 39, wherein the disease is cancer.

41. The method of claim 40, wherein the cancer is selected from the group consisting of melanoma, colon cancer, breast cancer and renal carcinoma.

42. The method of 40, wherein the cancer is metastatic melanoma.

43. The method of claim 40, 41, or 42 wherein the antibody is administered in combination concurrently or sequentially with a cytotoxic agent.

44. The method of claim 43 wherein the cytotoxic agent is dacarbazine.

45. The method of claim 39, wherein the human antibody is conjugated to or formulated with a therapeutic agent.

46. The method of claim 45 wherein the therapeutic agent is a cytotoxin.

47. A method according to any one of claims 39-46, wherein said administrating is by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracelebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal.

48. A method according to any one of claims 39-46, further comprising administering, prior, concurrently or after said antibody, at least one composition comprising an effective amount of at least one compound or protein selected from at least one of a detectable label or reporter, an anti-neoplastic agent, a TNF antagonist, an antirheumatic, a muscle relaxant, a narcotic, a non-steroid anti-inflammatory drug (NSAID), an analgesic, an anesthetic, a sedative, a local anethetic, a neuromuscular blocker, an antimicrobial, an antipsoriatic, a corticosteriod, an anabolic steroid, an erythropoietin, an immunization, an immunoglobulin, an immunosuppressive, a growth hormone, a hormone antagonist, a reproductive hormone antagonist, a hormone release modulator, a hormone replacement drug, , an antidepressant, an

antipsychotic, a stimulant, an asthma medication, a beta agonist, an inhaled steroid, an epinephrine or analog, a cytokine, or a cytokine antagonist.

49. A method according to claim 48 wherein the antibody is combined with an anti-neoplastic agent selected from a radiopharmaceutical, an estrogen receptor modulator, a retinoid, a topoisomererase inhibitor, a cytotoxin, an alkylating agent, a nitrogen mustard, a nitrosourea , an antimetabolite, a mitotic inhibitor, and a radiosensitizer.

50. A method according to claim 49 wherein the anti-neoplastic agent is dacarbazine.

51. A medical device, comprising at least one isolated human anti-alpha-V subunit antibody according to any one of claims 1-18, wherein said device is suitable to contacting or administerting said at least one anti-alpha-V subunit antibody by at least one mode selected from parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracelebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal.

52. An article of manufacture for human pharmaceutical or diagnostic use, comprising packaging material and a container comprising a solution or a lyophilized form of at least one isolated human anti-alpha-V subunit antibody according to any one of claims 1-18.

53. The article of manufacture of claim 52, wherein said container is a component of a parenteral, subcutaneous, intramuscular, intravenous, intrarticular, intrabronchial, intraabdominal, intracapsular, intracartilaginous, intracavitary, intracelial, intracelebellar, intracerebroventricular, intracolic, intracervical, intragastric, intrahepatic, intramyocardial, intraosteal, intrapelvic, intrapericardiac, intraperitoneal, intrapleural, intraprostatic, intrapulmonary, intrarectal, intrarenal, intraretinal, intraspinal, intrasynovial, intrathoracic, intrauterine, intravesical, bolus, vaginal, rectal, buccal, sublingual, intranasal, or transdermal delivery device or system.

54. A method for producing at least one isolated human anti-alpha v integrin subumit antibody according to any one of claims 1-18, comprising transfecting a host cell or transgenic animal or transgenic plant or plant cell capable of expressing in recoverable amounts said

antibody with a nucleic acid molecule encoding such antibody and recovering the antibody from cell, animal or plant.

55. At least one anti-alpha-V subunit antibody produced by a method according to claim 54.

56. At least one isolated mammalian anti-alpha-V subunit antibody that binds to the same epitope of an alpha-V subunit protein as an antibody according to any one of claims 1-18.

57. An alpha-V subunit antibody according to claim 56, wherein said antibody binds alpha-V subunit with an affinity of at least one selected from at least 10^{-9} M, at least 10^{-10} M, at least 10^{-11} M, or at least 10^{-12} M.

58. An alpha-V subunit antibody according to claim 56, wherein said antibody substantially neutralizes at least one activity of at least one alpha-V subunit protein.

59. An isolated nucleic acid encoding at least one isolated mammalian anti-alpha-V subunit antibody that binds to the same epitope of an alpha-V subunit protein as an antibody according to any one of claims 1-18.

60. An isolated nucleic acid encoding at least one isolated mammalian anti-alpha-V subunit antibody that binds to the same epitope of an alpha-V subunit protein as an antibody according to any one of claims 1-18, wherein the sequence of the nucleic acid comprises SEQ ID Nos: 18 or 19.

61. An isolated nucleic acid vector comprising an isolated nucleic acid according to claim 59 or 60.

62. A prokaryotic or eukaryotic host cell comprising an isolated nucleic acid according to claim 59 or 60.

63. A host cell according to claim 62, wherein said host cell is at least one selected from COS-1, COS-7, HEK293, BHK21, CHO, BSC-1, Hep G2, 653, SP2/0, 293, HeLa, myeloma, or lymphoma cells, or any derivative, immortalized or transformed cell thereof.

64. An anti-idiotype antibody or fragment that specifically binds at least one isolated human anti-alpha-V subunit antibody according to any one of claims 1-18.

65. An isolated nucleic acid encoding at least one isolated anti-alpha-V subunit antibody comprising a nucleic acid sequence according to SEQ ID NO:18 or 19.

66. A prokaryotic or eukaryotic host cell comprising an isolated nucleic acid according to claim 65.

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